REMARKS

Reconsideration and allowance are respectfully requested.

Claims 15 and 23-39 are pending. Applicants affirm election of Group I (claims 1-16) in response to the Examiner's restriction requirement. New claims 23-39 are drawn to the elected subject matter.

Non-elected claims 17-22 were withdrawn from consideration by the Examiner. Applicants have canceled the non-elected claims without prejudice to future prosecution of that subject matter.

The amendments are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, he is respectfully requested to point out the challenged limitation with particularity in the next Action so support may be cited in response.

An Abstract of the Disclosure on a separate sheet is submitted herewith.

The numbering of the drawings has been changed to conform to their description on page 30 of the specification. The Examiner's approval is requested for the indicated drawing change.

35 U.S.C. 101 – Utility

Claims 1-13 were rejected under Section 101 because "use" claims not setting forth a step involved in the process are allegedly informal. Applicants traverse. Based on the original claims (see especially claim 16) and page 23, lines 28-32, of the specification, new claims have been added to conform to U.S. practice. No objection was raised to claim 16 on this ground.

Withdrawal of the Section 101 rejection is requested because the pending claims are not informal.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up

assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-16 were rejected under Section 112, first paragraph, as allegedly not enabled by the specification. Applicants traverse.

The Examiner states, "Claims 1-15 are limited in their ultimate use to gene therapy, e.g. the method of claim 16, and the specification must enable the use of the claimed products for gene therapy." In response, the following comments address the issues raised on pages 9-13 of the Office Action. Together with the guidance provided by the supporting Examples, Applicants submit that the specification enables the skilled person to practice the invention and thus overcome the problems referred to in Orkin et al. as cited by the Examiner:

(i) Guidance as to use of nucleic acid, vectors and carriers etc. is provided on pages 14-20 of the specification. The use of nucleic acids, vectors and carriers in accordance with the present invention are described in detail therein. Page 14, line 31, to page 16, line 22, describes the vectors and how to use them. Page 16, line 24, to page 17, line 30, describes how the expression constructs "may be used": e.g., how expression vectors capable *in situ* of synthesizing NAB1 or NAB2 may be introduced into a wound site directly by physical methods. Finally, examples of suitable expression constructs (page 18, lines 17-35), host cells, vectors and promoters (page 19, line 8, to page 20, line 25) are provided. As referenced in the specification, molecular biology techniques used in the invention, for example, how to insert nucleic acid into the vector are well known in the art, see for example Sambrook et al. (cited in the specification on page 18, lines 1-15), and would therefore be available to the skilled person. Therefore, it is submitted that the specification does not merely list the various nucleic acids, prior art vectors and carriers that could be used but also teaches how they should be used.

(ii) Guidance as to where the compositions should be delivered relative to the wound site is provided throughout the specification. There is a general statement on page 14, lines 27-29, that the compositions should be administered to a wound site or to other tissues in need of healing. This is followed by a more detailed description on page 15, line 30, to page 16, line 5. For example, with reference to "gene gun technology" it is

explained that particles coated with the vector should be accelerated at speeds sufficient to enable them to penetrate the surface at the wound site, e.g., skin cells (page 16, lines 3-4). Administration to different types of wound sites is addressed in the context of pharmaceutical compositions (page 28, lines 17-20). The specification repeatedly states that the nucleic acid is to be administered (directly) to the wound site: see for example page 16, lines 18-19; page 16, line 26; page 16, line 28; and page 17, lines 6-7. Therefore, the claims have been amended to specify that administration is "to a wound site" in accordance with the Examiner's comment on page 12, lines 17-18, of the Office Action.

(iii) Guidance as to when the compositions should be delivered relative to when the wound was made is provided by statements in the specification that the technology has an application during healing and specifically refers to Shah et al. in this context (page 4, lines 4-5). Therefore, the skilled person would refer to the teachings of Shah et al. together with the specification of the present invention in determining when the compositions should be delivered. It is submitted that it would be obvious to the skilled person that in order to reduce scar tissue that the compositions should be delivered early in the healing process in order to have the desired effect. In addition to administration of NAB1/NAB2 after wounding, the specification teaches that the composition can be administered prior to wounding (Example 4). It is therefore submitted that the skilled person would be able to practice the invention from the teachings provided in the specification.

(iv) Guidance as to how much nucleic acid should be delivered is provided on page 29, lines 3-11, which provides dose ranges, and is supported by the Example on page 33, lines 4-14. The problem of preventing healing is also addressed when the dose is discussed, see last sentence on page 29, lines 9-11 which states, "Ultimately, the dose selected by the skilled person will have the function of reducing cell proliferation without preventing wound healing." This is also taken into consideration in Example 4, see page 35, lines 33-34, which concludes that the rate of healing is not impaired. Therefore, it is submitted that the specification does provide guidance as to how much nucleic acid should be delivered and does address the implication of reducing Egr-1 mediated transcription and cytokine production to levels below that of undamaged tissue.

It was questioned how Example 4 applies to a real-life situation because NAB nucleic acid was administered 24 hours before the wound was made. In response, it is submitted that Example 4 applies directly to a real-life situation where wounding occurs by surgery (e.g., cosmetic surgery on page 3, lines 19-20). It also demonstrates the general concept of using NAB nucleic acid to reduce scar tissue formation in wound healing as a result of the combination of effects of a reduction in TGFβ3 1, an increase in TGFβ3 and reduced angiogenesis (compared to the gold treated wounds). Therefore, it is submitted that these results do support the method of treatment provided by the invention.

For the reasons described above, the specification adequately describes where, when and how the compositions should be delivered to the wound site, in order to enable the skilled person to practice the invention. Therefore, it is submitted that the requirements of 35 U.S.C. 112, first paragraph, are met.

35 U.S.C. 112 – Definiteness

Claims 1-13 and 16 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The rejected claims have been canceled and the new claims that replace them recite an active, positive step in terms of how the invention is practiced. The limitation "the mammal is human" is recited in a dependent claim.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty

Claims 1-9 and 11-15 were rejected under Section 102(b) as allegedly being anticipated by Russo et al. (Proc. Natl. Acad. Sci. USA 92:6873-6877, 1995). Applicants traverse. Russo et al. disclose a mammalian expression vector comprising a coding sequence for the mouse NAB1 protein operatively linked to a CMV promoter and a process for making it (page 6873, col. 1; page 6875, Fig. 2 and col. 1).

Claims 1-9 and 11-15 were rejected under Section 102(b) as allegedly being anticipated by Svaren et al. (Mol. Cell. Biol. 16:6545-6553, 1996). Applicants traverse. Svaren et al. disclose a mammalian expression vector comprising a coding sequence for the mouse or human NAB2 proteins operatively linked to a CMV promoter and a process for making them (page 3546). Svaren et al. is cited by the Applicants on page 31, lines 1-3.

The Examiner states that recitation of an intended use of the nucleic acid composition does not distinguish the claimed products over the prior art products, which were used for transfecting cultured mammalian cells. But the pending claims are directed to methods of treatment and it is submitted that they relate to a novel invention. Neither Russo et al. nor Svaren et al. describe a method of treating cell proliferation disorders associated with wound healing. There is no suggestion that NAB nucleic acids could be used in gene therapy let alone to reduce scarring in either of these references. Therefore, it is submitted that the present claims are novel and inventive over the disclosures of Russo et al. and Svaren et al. It is also noted that claim 16 directed to a method of treatment was not rejected for lacking novelty.

Withdrawal of the Section 102 rejection is requested because all limitations of the claimed invention are not disclosed by the cited references.

35 U.S.C. 103 – Nonobviousness

Claims 1 and 10 were rejected under Section 103(a) as allegedly being unpatentable over either Russo et al. or Svaren et al. as applied to claims 1-9 and 11-15, and further in view of Sanford et al. (U.S. Patent 5,036,006). Applicants traverse because it is submitted that this rejection has been overcome by the amendment to the method of treatment claims for the reasons described above. A method of treating cell proliferation disorders associated with wound healing is not even suggested by the references.

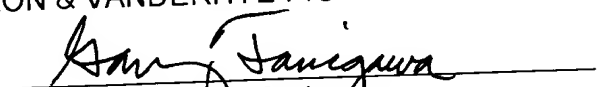
Withdrawal of the Section 103 rejection is requested because the invention as claimed was not obvious to a person of ordinary skill in the art at the time it was made.

Conclusion

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 6), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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APPENDIX
MARKED-UP VERSION TO SHOW CHANGES

IN THE CLAIMS

The claims are amended as follows.

15. (Amended) A method of treatment of cell proliferation disorders associated with wound healing in a mammal, which method comprises administration to a wound site of the mammal a pharmaceutical composition comprising a nucleic acid molecule comprising a sequence encoding an NAB1 or NAB2 polypeptide, or a biologically active fragment thereof, together with one or more pharmaceutically acceptable carriers thereof.

Claims 1-14 and 16-22 are canceled without prejudice or disclaimer, and claims 23-39 are added as new claims.

IN THE ABSTRACT

The Abstract of the Disclosure is amended as follows:

The invention relates to a method for treatment of cell proliferation disorders associated with wound healing in a mammal, which method comprises administration to a wound site of the mammal a nucleic acid molecule comprising a sequence encoding [the use, particularly in gene therapy, of] an NAB1 or NAB2 polypeptide or a biologically active fragment thereof[, and to nucleic acid molecules encoding such polypeptides, in the manufacture of a medicament for the treatment of cell proliferation disorders associated with wound healing in a mammal, including human].

IN THE DRAWINGS

The drawings are amended as shown in red on the attached.

Revise "Figure 2a" to read --Figure 2--.

Revise "Figure 3a" to read --Figure 3--.